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connected containers --

REMARKS

Claims 1, 4-5, 7-8, 11-12, 14-15 and 59-73 were pending in the subject application. By this Amendment applicants have canceled claims 1, 4-5, 7-8, 11-12, 14-15 and 59-73 without prejudice or disclaimer and added new claims 74-92. Accordingly, upon entry of this Amendment, claims 74-92 will be pending and under examination.

Applicants maintain that new claims 74-92 raise no issue of new matter and are fully supported by the specification as filed. Support for new claim 74 may be found inter alia in the specification, as originally-filed, on page 15, line 10 through page 16, line 32; page 18, line 27 through page 19, line 9; page 20, lines 1-10; page 22, lines 1-10; page 36, line 1 through page 37, line 32; page 12, lines 1-30; and Figures 1-3. Support for new claim 75 may be found inter alia in the specification, as originally-filed, on page 17, lines 15-21. Support for new claim 76 may be found inter alia in the specification, as originally-filed, on page 18, lines 6-11. Support for new claims 77 and 78 may be found inter alia in the specification, as originally-filed, on page 18, line 23 through page 19, line 9; page 43, line 16 through page 44, line 14; and Figure 5. Support for new claims 79 and 80 may be found inter alia in the specification, as originally-filed, on page 17, lines 23-33. Support for new claims 81-83 may be found inter alia in the specification, as originally-filed, on page 18, lines 13-22. Support for new claim 84 may be found inter alia in the specification, as originally-filed, on page 18, line 28 through page 19, line 9. Support for new claim 85 may be found inter alia in the specification, as

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originally-filed, on page 19, lines 10-16. Support for new claims 86-90 may be found inter alia in the specification, as originally-filed, on page 19, line 18 through page 23, line 4. Support for new claim 91 may be found inter alia in the specification, as originally-filed, on page 23, lines 5-7. Support for new claim 92 may be found inter alia in the specification, as originally-filed, on page 23, lines 9-11; page 37, lines 4-25; and Figure 1. Accordingly, applicants respectfully request that the Amendment be entered.

Rejections under 35 U.S.C. §112, second paragraph

On page 2 of the April 3, 2002 Office Action, the Examiner rejected claims 4 and 73 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

The Examiner stated that claim 4 is rejected over the use of improper Markush language, and that the phrase, "selected from the group consisting of" is suggested.

The Examiner stated that claim 73 provides for the use of method of detecting DNA sequence for detection of SNPs and different diseases and/or purposes, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicants are intending to encompass. The Examiner further stated that a claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

In response, in order to expedite the prosecution of the subject application, but without conceding the correctness of the

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Examiner's position, applicants have canceled claims 4 and 73, and added new claim 75 which incorporated the amendment suggested by the Examiner in connection with claim 4.

In view of the amendments made herein above, applicants respectfully request that the Examiner withdraw this ground of rejection.

Rejection under 35 U.S.C. §101

On page 3 of the Office Action, the Examiner rejected claim 73 under 35 U.S.C. §101 allegedly because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. §101.

In response, in order to expedite the prosecution of the subject application, but without conceding the correctness of the Examiner's position, applicants have canceled claim 73 thereby rendering this ground of rejection moot.

Obviousness-type double patenting rejection

On page 3 of the Office Action, the Examiner rejected claims 1, 4, 5, 8, 14, 15, 59-62, and 65 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-22 of U.S. Patent No. 6,046,005 (Ju and Konrad). The Examiner stated that although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-22 of U.S. Patent No. 6,046,005 disclose basically and fundamentally the same method of instant claims 1, 4, 5, 8, 14, 15, 59-62, and 65, for sequencing DNA by detecting the identity of a dideoxynucleotide incorporated at the

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3' end of a DNA sequencing fragment using mass spectrometry. The Examiner alleged that the basic steps of detection of DNA of the instant claims are the same as claims 1-22 of U.S. Patent No. 6,046,005, which comprises a) attaching a chemical moiety via a linker to a dideoxynucleotide, b) terminating a DNA sequencing reaction with the labeled dideoxynucleotide, c) capturing the labeled DNA sequencing fragment on a solid surface, d) washing the surface, e) freeing the DNA sequencing fragment from the surface, and f) analyzing the fragment using mass spectrometry so as to sequence the DNA.

In response, applicants maintain that the obviousness-type double patenting rejection is not a proper rejection in the instant case because although U.S. Patent No. 6,046,005 and the subject application share a common inventor, U.S. Patent No. 6,046,005 and the subject application are not commonly owned. Accordingly, applicants request that the Examiner withdraw this ground of rejection.

As a further response, in order to expedite the prosecution of the subject application, but without conceding the correctness of the Examiner's position, applicants have canceled claims 1, 4, 5, 8, 14, 15, 59-62, and 65 without prejudice or disclaimer, and added new claims 74-92 as set forth hereinabove. New claim 74 recites a method which comprises the use of either labeled dideoxynucleotides selected from a specific group of biotinylated dideoxynucleotides or a linker selected from a specific group of linkers. As discussed in the subject application (e.g., pages 39, line 6 through page 40, line 15, Table 1; page 42, line 1 through page 43, line 31), these features of the method are important for increasing mass separation between different labeled dideoxynucleotides and thereby increasing mass spectrometry resolution. The remaining pending claims are

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dependent on claim 74.

Applicants maintain that U.S. Patent No. 6,046,005 does not teach or suggest the specific biotinylated dideoxynucleotides and specific linkers recited in claim 74 and that the invention claimed in the subject application is not obvious over U.S. Patent No. 6,046,005.

Rejection under 35 U.S.C. §102(e)

On page 5 of the Office Action, the Examiner rejected claims 1, 4-5, 7-8, 14-15, 59-63, and 65-72 under 35 U.S.C. §102(e) as being anticipated by Ju and Konrad, U.S. Patent 6,046,005, issued April 4, 2000.

The Examiner alleged that Ju et al. teach a method for sequencing DNA by detecting the identity of a single or plurality of dideoxynucleotide incorporated to the 3' end of a DNA sequencing fragment using mass spectrometry (Abstract and Claims 1, 14, and 15, Figure 1 and Experimental Section), which comprises:

- a) attaching a chemical moiety via a linker to a dideoxynucleotide to produce a labeled dideoxynucleotide (Claims 1 and 15);
- b) terminating a DNA sequencing reaction with the labeled dideoxynucleotide to generate a labeled DNA sequencing fragment having a 3' end, and the chemical moiety is attached via the linker to the 3' end of the DNA sequencing fragment (Claims 1 and 15 and Figure 1);
- c) capturing the labeled DNA sequencing fragment on a surface coated with a compound that specifically interacts with the chemical moiety attached via the linker to the DNA sequencing fragment, thereby capturing the DNA sequencing fragment (Claims 1 and 15);

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- d) washing the surface to remove any non-bound component (Claims 1 and 15 and Experimental Section);
- e) freeing the DNA sequencing fragment from the surface by disrupting and cleaving the interaction between the chemical moiety attached via the linker to the DNA sequencing fragment and the compound on the surface (Claims 1 and 15 and Experimental Section and Figures 9-10); and
- f) analyzing the DNA sequencing fragment using mass spectrometry so as to sequence the DNA (Claim 14).

The Examiner further alleged the following: that Ju et al. teach a method, wherein the interaction between the chemical moiety attached via the linker to the DNA sequencing fragment and the compound on the surface comprises a biotin-streptavidin interaction (Claims 19-20 and Experimental Section); that Ju et al. teach a method, wherein the dideoxynucleotide comprises a cytosine or thymine with a 5-position and the linker is attached to the 5-position of cytosine or thymine (Figure 8 and Experimental Section); that Ju et al. teach a method, wherein a plurality of different linkers is used to increase mass separation between different labeled DNA sequencing fragments and thereby increase mass spectrometry resolution (Column 7, lines 1-9 and column 9, lines 15-32); that Ju et al. teach a method, wherein the interaction of the linker is cleaved by ultraviolet light (Figures 9-10); that Ju et al. teach a method, wherein the chemical moiety comprises biotin, the labeled dideoxynucleotide is a biotinylated dideoxynucleotide, and the surface is a streptavidin-coated magnetic bead solid surface (Figure 1 and Experimental Section and Claim 20); that Ju et al. teach a method, wherein the biotinylated dideoxynucleotide is selected from ddATP-11-biotin, ddCTP-11-biotin, ddGTP-11-biotin, ddTTP-11-biotin and the compounds of claims 67-70 (Column 6, lines 35-64 and Figures 8-10); and that Ju et al. teach a method, wherein the

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steps (b) to (e) are performed in a plurality of connected containers (Experimental Section).

In response, in order to expedite the prosecution of the subject application, but without conceding the correctness of the Examiner's position, applicants have canceled claims 1, 4-5, 7-8, 14-15, 59-63, and 65-72 without prejudice or disclaimer, and added new claims 74-92 as set forth hereinabove. New claim 74 recites a method which comprises the use of either labeled dideoxynucleotides selected from a specific group of biotinylated dideoxynucleotides or a linker selected from a specific group of linkers. New claims 75-92 are dependent on claim 74.

Applicants maintain that U.S. Patent No. 6,046,005 does not teach or suggest the specific biotinylated dideoxynucleotides and specific linkers recited in claim 74, and that the invention claimed in the subject application is not anticipated by U.S. Patent No. 6,046,005. Accordingly, in view of the amendments and remarks made hereinabove, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Rejection under 35 U.S.C. §103(a)

On page 8 of the Office Action, the Examiner rejected claims Claims 1, 4-5, 7-8, 11-12, 14-15, and 59-72 under 35 U.S.C. §103(a) over Ju and Konrad (U.S. Patent 6,046,005, issued April 4, 2000) in view of Arbo et al. (International Journal of Peptide and Protein Research, (1993), Vol. 42, pages 138-154).

The Examiner alleged that Ju et al. teach the method of claims of 1, 4-5, 7-8, 14-15, and 59-63, and 65-72 as described above including any linkers comprising a photo or chemically cleavable moiety. The Examiner stated that Ju et al. do not teach a

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method, wherein the cleavable linkers are a derivative of 4-aminomethyl benzoic acid containing fluorine. The Examiner stated that Arbo et al. teach a method, wherein the cleavable linkers are a derivative of 4-aminomethyl benzoic acid containing fluorine (Abstract and page 149, Column 2 to page 151, Column 1).

The Examiner alleged that it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the chemically equivalent cleavable linkers, which are a derivative of 4-aminomethyl benzoic acid containing fluorine of Arbo et al. in the method of Ju et al., since Ju et al. state, "In such linkers, the linker will comprise a cleavable moiety that is either photo or chemically cleavable (Column 7, lines 1-3)." The Examiner alleged that by employing scientific reasoning, an ordinary practitioner would have been motivated to combine and substitute the chemically equivalent cleavable linkers, which are a derivative of 4-aminomethyl benzoic acid containing fluorine of Arbo et al. in the method of Ju et al., in order to achieve the express advantages, as noted by Ju et al., of linkers which will comprise a cleavable moiety that is either photo or chemically cleavable.

In response, in order to expedite the prosecution of the subject application, but without conceding the correctness of the Examiner's position, applicants have canceled claims 1, 4-5, 7-8, 14-15, 59-63, and 65-72 without prejudice or disclaimer, and added new claims 74-92 as set forth hereinabove. New claim 74 recites a method which comprises the use of either labeled dideoxynucleotides selected from a specific group of biotinylated dideoxynucleotides or a linker selected from a specific group of linkers. New claims 75-92 are dependent on claim 74. Applicants further note that new claim 77 recites that the linker "comprises

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a derivative of 4-aminomethyl benzoic acid containing a carbon-carbon triple bond."

Applicants maintain that neither U.S. Patent No. 6,046,005 nor Arbo et al. (International Journal of Peptide and Protein Research, (1993), Vol. 42, pages 138-154) teach or suggest the specific biotinylated dideoxynucleotides and specific linkers recited in claim 74. Applicants also maintain that Arbo et al. do not teach or suggest a linker which comprises a derivative of 4-aminomethyl benzoic acid containing a carbon-carbon triple bond. Applicants further maintain that the invention claimed in the subject application is not obvious over Ju et al. in view of Arbo et al. Accordingly, in view of the amendments and remarks made hereinabove, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Supplemental Information Disclosure Statement

This Supplemental Information Disclosure Statement is submitted under 37 C.F.R. § 1.97(c)(2) to supplement the Information Disclosure Statements filed on July 6, 2001.

According to 37 C.F.R. §1.97(c), an Information Disclosure Statement shall be considered by the U.S. Patent and Trademark Office if filed before the mailing date of any of a Final Office Action under 37 C.F.R. §1.113, a Notice of Allowance under 37 C.F.R. §1.311, or an action that otherwise closes prosecution in the application, if the Information Disclosure Statement is accompanied by either (1) a statement as specified in 37 C.F.R. §1.97(e) or (2) the fee set forth in C.F.R. §1.17(p). Applicants are filing this Supplemental Information Disclosure Statement before the issuance of a Final Office Action, a Notice of Allowance, or an action closing prosecution in the subject

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application. The fee set forth in C.F.R. §1.17(p) is ONE HUNDRED EIGHTY DOLLAR (\$180.00) and a check including this amount is enclosed.

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants would like to direct the Examiner's attention to the following references which are listed on the attached Form PTO-1449 (**Exhibit 1**) and attached hereto as **Exhibits 2-4**:

1. PCT International Publication No. WO 02/29003, published April 11, 2002 (**Exhibit 2**);
2. U.S. Serial No. 09/972,364, filed October 5, 2001, Ju et al. (**Exhibit 3**); and
3. U.S. Serial No. 10/194,882, filed July 12, 2002, Ju (**Exhibit 4**).

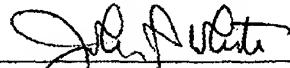
In summary, in view of the amendments and remarks made hereinabove, applicants request that the Examiner withdraw the various grounds of rejection set forth in the April 3, 2002 Office Action and earnestly solicit allowance of all claims now pending in the subject application, i.e. claims 74-92.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone the number provided below.

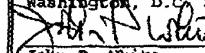
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No fee, other than the enclosed \$380.00 fee (\$200.00 fee for a two month extension of time plus \$180.00 for filing an Information Disclosure Statement), is deemed necessary in connection with the filing of this Amendment and Supplemental Information Disclosure Statement. However, if an additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.	
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